REMARKS

Claims 1-5, 10-13, 15, 17-21 and 23-47 are pending in the application. Claims 6-9, 14, 16 and 22 are cancelled. Claims 2-4, 12-13, 15, 20-21, 24-25, 27-30, 33-38, and 44-45 are listed by the Examiner as withdrawn. Thus, Claims 1, 5, 10, 11, 17-19, 23, 26, 31, 32, 39-43, 46 and 47 are presently under examination.

Rejection Under 35 U.S.C. 112, Second Paragraph

Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph.

According to the Office Action, claims 17 and 18 remain confusing, even with the amendment made to claim 1 in applicant's response dated February 9, 2010, because claim 17 recites that the therapeutic agent and microparticles are admixed together, while claim 1 requires the therapeutic agent and the microparticles are applied as separate entities, and the therapeutic agent is present between the microparticles, and not mixed with the microparticles.

The Office Action also states that claim 18 is confusing because the claim recites that microparticles are applied to the adhesive followed by application of the therapeutic agent, and this will create two layers and not the therapeutic agent and the microparticles applied as separate entities and the therapeutic agent is present between the microparticles as recited by claim 1.

With regard to claim 1, the Examiner's attention is directed to schematic Figs. 1A and 1B below. Fig. 1A is a top view of a medical article comprising an adhesive region (shown in gray), upon which are adhered microparticles (illustrated by nine large spheres) and a therapeutic agent (illustrated by numerous small spheres). Fig. 1B is a cross-section taken along line B---B of Fig. 1A and shows how the microparticles (large spheres) form pockets between them which are occupied by the therapeutic agent (small spheres).

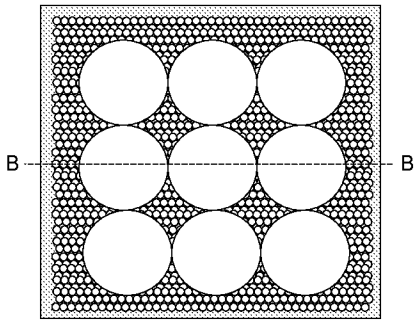

Fig. 1A

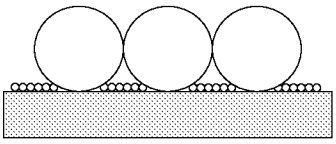
Fig. 1B

In claim 17, the medical article is provided by a process in which the therapeutic agent is admixed in powder form with the microparticles and applied to the adhesive region. This is consistent with claim 1. Clearly a mixture can be formed which comprises the therapeutic agent and the microparticles and which can be applied to the adhesive region.

With regard to the fact that claim 1 states that the therapeutic agent and the microparticles are applied to the surface of the adhesive region as separate entities, microparticles and therapeutic agent can clearly exist in a mixture as separate entities, for example, just as a jar of red and blue marbles exist as separate entities in an admixture. See also paragraph [0035] of the specification. It is further noted that claim 1 does *not* require that the therapeutic agent and the microparticles be applied to the surface of the adhesive region as separate entities *at different times (sequentially)*, which would understandably result in an internal inconsistency between claims 1 and 17.

In claim 18, the medical article is provided by a process in which the microparticles are applied to the adhesive region in powder form, followed by the application of the therapeutic agent in powder form. Such a method, however, is not inconsistent with claim 1, in which the therapeutic agent and the microparticles are applied to the surface of the adhesive region as separate entities and in which the microparticles create pockets between them which are occupied by the therapeutic agent and from which the therapeutic agent is released.

This can be shown using figures analogous to Figs. 1A and 1B above. For example, as shown in schematic Figs. 2A (top view) and 2B (cross-section taken along line B---B in Fig. 2A), microparticles (illustrated by nine large spheres in Fig. 2A) can first be applied to an adhesive region (shown in gray).

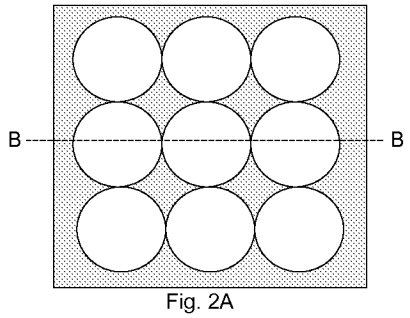

Fig. 2A

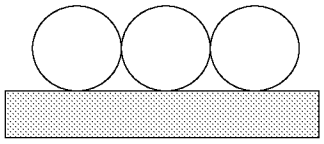

Fig. 2B

Subsequently, as shown in schematic Figs. 3A (top view) and 3B (cross-section taken along line B---B in Fig. 3A), therapeutic agent (illustrated by small spheres) can then be applied to the assembly shown in Figs. 2A-2B, such that the therapeutic agent occupies pockets **P** created between the microparticles as shown in Fig. 3 B. Such particles can reach the pockets through the spaces **S** between the larger microparticles as shown in Fig. 3 A.

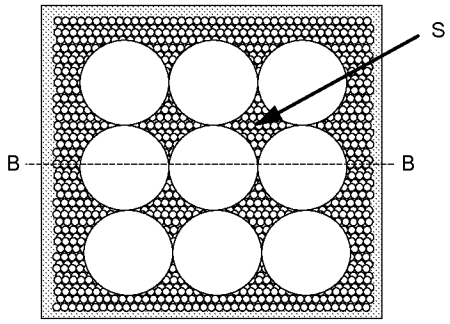

Fig. 3A

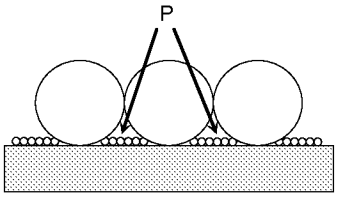

Fig. 3B

For at least the above reasons, reconsideration and withdrawal of the rejection of claims 17 and 18 under 35 U.S.C. 112, second paragraph, is requested.

Rejection Under 35 U.S.C. 103(a) – Harish in view of Pilliar

Claims 1, 5, 10, 11, 17-19, 23, 26, 31, 32, 39-43 and 46-47 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Harish et al., WO02/26162 (Harish) in view of Pilliar, U.S. 3,855,638 (Pilliar). Applicants respectfully traverse this rejection.

As noted in the Office Action, Harish teaches an implantable device coated on preselected regions/portions of its outer surface with therapeutic agent. The therapeutic agent is deposited on the surface of the device in the form of a dry stream of particles. The device is covered by a polymeric primer prior to applying the therapeutic particles to adhere the particles to the surface of the stent. The particles may be made of any substance suitable for loading onto

implantable devices in solid form, including, but not limited to therapeutic substances or agents, radioisotopes, radiopaque substances, polymers, proteins, and nucleic acids (page 8, 1st full paragraph). Lists of therapeutic substances, radioactive/radiopaque substances, polymeric materials (including bioabsorbable polymers, polymeric biomolecules, and biostable polymers), proteins and nucleic acids are found on pages 9-11. The particles can be spherical having diameter from about 5 to 20 microns. The layer containing the particles can be covered by a polymeric topcoat that helps immobilize the particles on the surface of the device and controls the release of the therapeutic agents from the surface of the device. Individual particles within the stream may or may not be of uniform composition, as individual particles within a stream may be made of the same substance(s) or of different substances (page 12, last paragraph).

The Office Action further argues that "[a]lthough Harish teaches therapeutic particles coated as dry powder on a stent by virtue of adhesive [primer layer], and further teaches the particles may be made of different substances including biostable substances, however, the reference does not explicitly teach the therapeutic agent and the microparticles are separate entities as instantly claimed by amended claim 1."

To make up for this deficiency, the Examiner turns to Pilliar. As noted in the Office Action, Pilliar teaches implantable devices partially coated with plurality of small discrete metallic particles bonded together at points of contact with each other to define a plurality of pores in the coating and adhere to the device. The coating provides the device with uniform strength through the thickness of the coating. The pores of the implant may be treated with therapeutic agent such as materials that promote the tissue growth or antibiotics before implantation.

To form such a porous coating, Pilliar further teaches that a slurry of metallic powder suspended in aqueous solution with organic binders is applied to a substrate and heated to remove the water and finally sintered in an inert or reducing atmosphere, such as hydrogen, *to burn off the organic binder* and fuse the particles together and to the substrate (col. 7, lines 37-40).

In the particular embodiment of Example 1, an aqueous VITALLIUM powder slurry (VITALLIUM is a cobalt alloy) containing atomized VITALLIUM powder, methylcellulose, dioctyl sodium sulfosuccinate and ammonium hydroxide was made up and applied to a VITALLIUM rod to a depth of 1/32 inch. After drying, the coated rod was sintered at 2,200°F

(i.e., white hot temperature) in a dry hydrogen atmosphere for approximately two hours, fusing the spherical powder particles at each contact point between themselves and the rod, and an interior communicating substantially uniform pore structure was evident.

On the basis of the above teachings the Office Action urges that the presently claimed invention is obvious, specifically arguing as follows (emphasis added):

> Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention ***to provide an implantable device coated with dry powdered particles of therapeutic agents and other biostable substances adhered to the surface of the device by primer*** as taught by Harish, and ***replace the particle of the other biostable substances with the metallic particles taught by Pilliar that adhere together to form pores***. One would have been motivated to do so because Pilliar teaches that partial coating of implantable device with metallic particles provides the implantable device with uniform strength. ***Further, one would have been motivated to apply therapeutic agent along with metallic particles*** because Pilliar teaches that pores formed by the metallic particles can be treated with therapeutic agents before implantation. ***One would reasonably expect formulating an implantable device coated with dry powdered particles of therapeutic agents and metallic particles that are adhered together forming pores and adhered to the surface of the device*** wherein the device has sufficient strength and controllably releases the particles of the therapeutic agents.

Applicant respectfully disagrees.

One would <u>not</u> have been motivated to apply a therapeutic agent along with the metallic particles to an adhesive region in order to form an implantable device coated with dry powdered particles of therapeutic agents and metallic particles that are adhered together forming pores and adhered to the surface of the device.

Moreover, one would <u>not</u> have arrived at the presently claimed invention by doing so. In this regard, claim 1 requires a "medical article comprising: (a) an adhesive region comprising an adhesive; (b) a therapeutic agent, wherein at least a portion of said therapeutic agent is adhered to a surface of said adhesive region; and (c) microparticles, at least a portion of which are adhered to said surface of said adhesive region…"

This is true, because the adhesive region (i.e., prepolymer) taught by Harish and the therapeutic agents taught by Harish and Pilliar would be removed by the process of forming the porous coating that is taught by Pilliar. Specifically, the process taught by Pilliar involves heating a slurry of metallic powder suspended in aqueous solution with organic binders to remove the water, followed by sintering in an inert or reducing atmosphere, such as hydrogen, to

burn off the organic binder and fuse the particles together and to the substrate.[1] Such a process would clearly remove the prepolymer adhesive region taught by Harish. Such a process would remove as well the therapeutic agents taught by Harish and Pilliar. Consequently, one would not be motivated to carry out such a process and one would not arrive and the presently claimed invention by employing such a process.

For at least the above reasons, reconsideration and withdrawal of the rejection of the claims under 35 USC 103(a) are respectfully requested.

CONCLUSION

Applicants submit that the pending claims are in condition for allowance. Reconsideration and a Notice of Allowance are requested.

Should the Examiner be of the view that an interview would expedite consideration of this Response or of the application at large, the Examiner is requested to telephone the Applicant's attorney at the number listed below in order to resolve any outstanding issues in this case.

Respectfully submitted,

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[1] It is again noted that, in the Examples, a slurry coating is sintered at 2,200°F (i.e., ***white hot temperature***) in a dry hydrogen atmosphere for approximately two hours.